AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph on page 1, lines 2-9 with the following amended paragraph:

This application **is a continuation application of U.S. Serial No. 08/260,190 (filed June 15, 1994) which** is a continuation-in-part of ~~now pending~~ U.S. Serial No. 08/177,093 (filed December 30, 1993) **which issued on April 18, 2000 as U.S. Patent No. 6,051,226**, which is in turn a continuation-in-part of U.S. Serial No. 07/964,589 (filed October 21, 1992) **which issued on February 7, 1995 as U.S. Patent No. 5,387,676**. This application declares priority under 35 USC § 120 from those U.S. applications, and also under 35 USC § 119 from the now pending Czechoslovakian patent application PV-709-92 (filed March 11, 1992).

Please replace the paragraph on page 8, lines 3-11 with the following amended paragraph:

This invention also concerns nucleic acids which encode MN proteins or polypeptides that are specifically bound by monoclonal antibodies designated M75 that are produced by the hybridoma VU-M75 deposited at the American Type Culture Collection (ATCC) ~~at 12301 Parklawn Drive in Rockville, Maryland 20852~~ **10801 University Blvd., Manassas, Virginia 20110-2209** (USA) under ATCC No. HB 11128, and/or by monoclonal antibodies designated MN12 produced by the hybridoma MN 12.2.2 deposited at the ATCC under ATCC No. HB 11647.

Please replace the paragraph on page 13, lines 3-14 with the following amended paragraph:

A hybridoma that produces a representative MN-specific antibody, the monoclonal antibody M75 (Mab M75), was deposited at the ~~under ATCC~~ **ATCC under** Number HB 11128 as indicated above. The M75 antibody was used to discover and identify the MN protein and can be used to identify readily MN antigen in Western blots, in radioimmunoassays and immunohistochemically, for example, in tissue samples that are fresh, frozen, or formalin-, alcohol-, acetone- or otherwise fixed and/or paraffin-embedded and deparaffinized. Another representative MN-specific antibody, Mab MN12, is secreted by the hybridoma MN 12.2.2, which was deposited at the ATCC under the designation HB 11647.

Please replace the paragraph on page 16, lines 3-10 with the following amended paragraph:

The immunoassays of this invention can be embodied in test kits which comprise MN proteins/polypeptides and/or MN-specific antibodies. Such test kits can be in solid phase formats, but are not limited thereto, and can also be in liquid phase format, and can be based on immunohistochemical assays, ~~ELISAS,~~ **ELISAs,** particle assays, radiometric or fluorometric assays either unamplified or amplified, using, for example, avidin/biotin technology.

Please replace line 26 on page 17 with the following amended line:

IPTG - ~~isopropyl-Beta~~ **isopropyl-beta**-D-thiogalacto-pyranoside

Please replace the paragraph bridges pages 27 and 28 with the following amended paragraph:

~~Figure 15~~ **Figure 15A-C** shows a complete nucleotide sequence of a MN cDNA [SEQ. ID. NO.: 5]. Also shown is the deduced amino acid sequence [SEQ. ID. NO.: 6]. The polyadenylation signal (AATAAA) and the mRNA instability motif (ATTTA) ~~are underlined~~ **are located at nucleotides (nts) 1507-1512 and at nts 1513-1518, respectively**. The amino acid residues of the putative signal peptide as well as the membrane-spanning segment are ~~italicized~~ **are located at amino acids (aa) 1-37 and at aa 415-433, respectively**. The N-glycosylation site ~~and the putative nuclear localization signal are denoted by squares and asterisks, respectively~~ **is located at aa 346**. The S/TPXX elements are ~~indicated with open circles~~ **are located at amino acids 7-10, 47-50, 71-74, 153-156, 162-165, 333-336, and 397-400**.

Please replace the paragraph on page 54, lines 14-20 with the following amended paragraph:

Where the host used is an ~~eucaryote,~~ **eukaryote,** transfection methods such as the use of a calcium phosphate-precipitate, electroporation, conventional mechanical procedures such as microinjection, insertion of a plasmid encapsulated in red blood cell ghosts or in liposomes, treatment of cells with

agents such as lysophosphatidyl-choline or use of virus vectors, or the like may be used.

Please replace the paragraph on page 54, lines 14-20 with the following amended paragraph:

The MN 20-19 protein was purified from the conditioned media by immunoaffinity chromatography. 6.5 mg of Mab M75 was coupled to 1 g of Tresyl activated Toyopearl™ [**solid support in bead form;** Tosoh, Japan (#14471)]. Approximately 150 ml of the conditioned media was run through the M75-Toyopearl column. The column was washed with PBS, and the MN 20-19 protein was eluted with 1.5 M MgCl. The eluted protein was then dialyzed against PBS.

Please replace the paragraph on page 86, lines 10-16 with the following amended paragraph:

MAb M75. Monoclonal antibody M75 (MAb M75) is produced by mouse lymphocytic hybridoma VU-M75, which was initially deposited in the Collection of Hybridomas at the Institute of Virology, Slovak Academy of Sciences (Bratislava, ~~Czechoslovakia~~ **Slovakia**) and was deposited under ATCC Designation HB 11128 on September 17, 1992 at the American Type Culture Collection (ATCC) in ~~Rockville, MD~~ **Manassas, Virginia** (USA).

Please replace the paragraph on page 89, lines 9-20 with the following amended paragraph:

Mab MN12. Monoclonal antibody MN12 (Mab MN12) is produced by the mouse lymphocytic hybridoma MN 12.2.2 which was deposited under ATCC Designation HB 11647 on June 9, 1994 at the American Type Culture Collection (ATCC) at ~~12301 Parklawn Drive, Rockville, MD 20852~~ **10801 University Blvd., Manassas, Virginia 20110-2209** (USA). Antibodies corresponding to Mab MN12 can also be made, analogously to the method outlined above for Mab MN9, by screening a series of antibodies prepared against an MN protein/polypeptide, against the peptide representing the epitope for Mab MN12. That peptide is Gly Lys Met Thr His Trp [SEQ. ID. NO.: 11]. The Novatope system could also be used to find antibodies specific for said epitope.

Please delete line 23 on page 91:

~~Antisense MN Nucleic Acid Sequences~~

Please replace the paragraph bridges pages 94 and 95 with the following amended paragraph:

MN proteins and/or polypeptides may be synthesized or prepared recombinantly or otherwise biologically, to comprise one or more amino acid sequences corresponding to one or more epitopes of the MN proteins either in monomeric or multimeric form. Those proteins and/or polypeptides may then be incorporated into vaccines capable of inducing protective immunity. Techniques for enhancing the antigenicity of such

polypeptides include incorporation into a multimeric structure, binding to a highly immunogenic protein carrier, for example, keyhole limpet hemocyanin (KLH), or ~~diptheria~~ **diphtheria** toxoid, and administration in combination with adjuvants or any other enhancers of immune response.

Please replace the paragraph bridges pages 95 and 96 with the following amended paragraph:

An amino acid sequence corresponding to an epitope of an MN protein/polypeptide either in monomeric or multimeric form may also be obtained by chemical synthetic means or by purification from biological sources including genetically modified microorganisms or their culture media. [See Lerner, "Synthetic Vaccines", Sci. Am. 248(2): 66-74 (1983).] The protein/polypeptide may be combined in an amino acid sequence with other proteins/polypeptides including fragments of other proteins, as for example, when synthesized as a fusion protein, or linked to other antigenic or ~~non-antigeneic~~ **non-antigenic** polypeptides of synthetic or biological origin. In some instances, it may be desirable to fuse a MN protein or polypeptide to an immunogenic and/or antigenic protein or polypeptide, for example, to stimulate efficacy of a MN-based vaccine.

Please replace the two paragraphs on page 98, lines 11-24 with the following amended paragraphs:

Human sera from cancer patients, from patients suffering with various non-tumor complaints and from healthy

women were obtained from the Clinics of Obstetrics and Gynaecology at the Postgraduate Medical School, Bratislava, ~~Czechoslovakia~~ **Slovakia**. Human ~~sera~~ **serum** KH was from a fifty year old mammary carcinoma patient, fourteen months after resection. That serum was one of two sera out of 401 serum samples that contained neutralizing antibodies to the VSV(MaTU) pseudotype as described in Zavada et al. (1972), supra. Serum L8 was from a patient with Paget's disease. Serum M7 was from a healthy donor.

Rabbit anti-MaTu serum was prepared by immunizing a rabbit three times at intervals of 30 ~~days with 10-5~~ **days with 1-5** x 10^7 viable MaTu-infected HeLa cells.

Please replace the paragraph on page 107, lines 4-11 with the following amended paragraph:

A ~~radimmunoassay~~ **radioimmunoassay** was performed directly in confluent petri dish (5 cm) culture of cells, fixed with methanol essentially as described in Example 3, supra. The monolayers were fixed with methanol and treated with ^{125}I-labeled MAbs M67 (specific for exogenous MX antigen) or M75 (specific for endogenous MN antigen) at 6 x 10^4 cpm/dish. The bound radioactivity was measured; the results are shown in Figure 6.

Please replace the paragraph bridging pages 119 and 120 with the following amended paragraph:

It was found that cultivation of HeLa cells with the ODNs resulted in considerable inhibition of p54/58N synthesis.

The 19-mer ODN2 (Figure 3B) in 4 μM final concentration was very effective; as determined by RIA, it caused 40% inhibition, whereas the 29-mer ODN1 (4 μM) (Figure 3A) and a combination of the two ODNs (Figure 3C), each in 2 μM final concentration, were less effective in RIA showing a 25-35% ~~increase~~ **decrease** of the MN-related proteins. At the same time, the amount of different HeLa cell protein determined by RIA using specific MAb H460 was in all cell variants approximately the same. Most importantly was that on immunoblot it could be seen that specific inhibition by the ODNs affected both of the p54/58N proteins. Thus, we concluded that the MN gene we cloned coded for both p54/58N proteins in HeLa cells.

Please replace TABLE 2 on page 131, lines 1-27 with the following amended TABLE 2:

TABLE 2

Immunoreactivity of M75 in Various Tissues

TISSUE	TYPE	POS/NEG (#pos/#tested)
liver, spleen, lung, kidney, adrenal gland, brain, prostate, pancreas, ~~thyroid ovary,~~ **thyroid, ovary,** testis	normal	NEG (all)
skin	normal	POS (in basal layer) (1/1)
stomach	normal	POS
small intestine	normal	POS
colon	normal	POS
breast	normal	NEG (0/10)
cervix	normal	NEG (0/2)
breast	benign	NEG (0/17)
colon	benign	POS (4/11)
cervix	benign	POS (10/18)
breast	malignant	POS (3/25)
colon	malignant	POS (9/15)
ovarian	malignant	POS (3/15)
lung	malignant	POS (12/30)
bladder	malignant	POS (1/3)
head & neck	malignant	POS (3/4)
kidney	malignant	POS (4/4)
stomach	malignant	NEG (0/4)
cervix	malignant	POS (62/68)

Please replace the paragraph bridging pages 141 and 142 with the following amended paragraph:

ATCC Deposits. The material listed below was deposited with the American Type Culture Collection (ATCC) at ~~12301 Parklawn Drive, Rockville, MD 20852~~ **10801 University Blvd., Manassas, Virginia 20110-2209** (USA). The deposits were made

under the provisions of the Budapest Treaty on the International Recognition of Deposited Microorganisms for the Purposes of Patent Procedure and Regulations thereunder (Budapest Treaty). Maintenance of a viable culture is assured for thirty years from the date of deposit. The organism will be made available by the ATCC under the terms of the Budapest Treaty, and subject to an agreement between the Applicants and the ATCC which assures unrestricted availability of the deposited hybridomas to the public upon the granting of patent from the instant application. Availability of the deposited strain is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any Government in accordance with its patent laws.

Page 143 After the Detailed Description, please insert the SEQUENCE LISTING:

SEQUENCE LISTING

<110> Zavada, Jan
Pastorekova, Silvia
Pastorek, Jaromir

<120> MN Gene and Protein

<130> D-0021.2-2

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tct ggg gaa gat gac cca ctg ggc gag gag gat ctg ccc agt gaa gag   96
Ser Gly Glu Asp Asp Pro Leu Gly Glu Glu Asp Leu Pro Ser Glu Glu
            20                  25                  30

gat tca ccc aga gag gag gat cca ccc gga gag gag gat cta cct gga   144
Asp Ser Pro Arg Glu Glu Asp Pro Pro Gly Glu Glu Asp Leu Pro Gly
        35                  40                  45

gag gag gat cta cct gga gag gag gat cta cct gaa gtt aag cct aaa   192
Glu Glu Asp Leu Pro Gly Glu Glu Asp Leu Pro Glu Val Lys Pro Lys
    50                  55                  60
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Ala Pro Gly Asp Pro Gln Glu Pro Gln Asn Asn Ala His Arg Asp Lys
                85                  90                  95

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Glu Gly Asp Asp Gln Ser His Trp Arg Tyr Gly Gly Asp Pro Pro Trp
            100                 105                 110

ccc cgg gtg tcc cca gcc tgc gcg ggc cgc ttc cag tcc ccg gtg gat   384
Pro Arg Val Ser Pro Ala Cys Ala Gly Arg Phe Gln Ser Pro Val Asp
        115                 120                 125

atc cgc ccc cag ctc gcc gcc ttc tgc ccg gcc ctg cgc ccc ctg gaa   432
Ile Arg Pro Gln Leu Ala Ala Phe Cys Pro Ala Leu Arg Pro Leu Glu
    130                 135                 140

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Leu Leu Gly Phe Gln Leu Pro Pro Leu Pro Glu Leu Arg Leu Arg Asn
145                 150                 155                 160

aat ggc cac agt gtg caa ctg acc ctg cct cct ggg cta gag atg gct   528
Asn Gly His Ser Val Gln Leu Thr Leu Pro Pro Gly Leu Glu Met Ala
                165                 170                 175

ctg ggt ccc ggg cgg gag tac cgg gct ctg cag ctg cat ctg cac tgg   576
Leu Gly Pro Gly Arg Glu Tyr Arg Ala Leu Gln Leu His Leu His Trp
            180                 185                 190

ggg gct gca ggt cgt ccg ggc tcg gag cac act gtg gaa ggc cac cgt   624
Gly Ala Ala Gly Arg Pro Gly Ser Glu His Thr Val Glu Gly His Arg
        195                 200                 205

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Phe Pro Ala Glu Ile His Val Val His Leu Ser Thr Ala Phe Ala Arg
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Val Asp Glu Ala Leu Gly Arg Pro Gly Gly Leu Ala Val Leu Ala Ala
225                 230                 235                 240

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Phe Leu Glu Glu Gly Pro Glu Glu Asn Ser Ala Tyr Glu Gln Leu Leu
                245                 250                 255

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Ser Arg Leu Glu Glu Ile Ala Glu Glu Gly Ser Glu Thr Gln Val Pro
            260                 265                 270

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Gly Leu Asp Ile Ser Ala Leu Leu Pro Ser Asp Phe Ser Arg Tyr Phe
        275                 280                 285

caa tat gag ggg tct ctg act aca ccg ccc tgt gcc cag ggt gtc atc   912
Gln Tyr Glu Gly Ser Leu Thr Thr Pro Pro Cys Ala Gln Gly Val Ile
    290                 295                 300

tgg act gtg ttt aac cag aca gtg atg ctg agt gct aag cag ctc cac   960
Trp Thr Val Phe Asn Gln Thr Val Met Leu Ser Ala Lys Gln Leu His
305                 310                 315                 320

acc ctc tct gac acc ctg tgg gga cct ggt gac tct cgg cta cag ctg  1008
Thr Leu Ser Asp Thr Leu Trp Gly Pro Gly Asp Ser Arg Leu Gln Leu
                325                 330                 335
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aac ttc cga gcg acg cag cct ttg aat ggg cga gtg att gag gcc tcc   1056
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            340                 345                 350

ttc cct gct gga gtg gac agc agt cct cgg gct gct gag cca gtc cag   1104
Phe Pro Ala Gly Val Asp Ser Ser Pro Arg Ala Ala Glu Pro Val Gln
        355                 360                 365

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Leu Asn Ser Cys Leu Ala Ala Gly Asp Ile Leu Ala Leu Val Phe Gly
    370                 375                 380

ctc ctt ttt gct gtc acc agc gtc gcg ttc ctt gtg cag atg aga agg   1200
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Gln His Arg Arg Gly Thr Lys Gly Gly Val Ser Tyr Arg Pro Ala Glu
                405                 410                 415

gta gcc gag act gga gcc tagaggctgg atcttggaga atgtgagaag          1296
Val Ala Glu Thr Gly Ala
            420

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Asp Ser Pro Arg Glu Glu Asp Pro Pro Gly Glu Glu Asp Leu Pro Gly
        35                  40                  45

Glu Glu Asp Leu Pro Gly Glu Glu Asp Leu Pro Glu Val Lys Pro Lys
    50                  55                  60

Ser Glu Glu Glu Gly Ser Leu Lys Leu Glu Asp Leu Pro Thr Val Glu
65                  70                  75                  80

Ala Pro Gly Asp Pro Gln Glu Pro Gln Asn Asn Ala His Arg Asp Lys
                85                  90                  95

Glu Gly Asp Asp Gln Ser His Trp Arg Tyr Gly Gly Asp Pro Pro Trp
            100                 105                 110

Pro Arg Val Ser Pro Ala Cys Ala Gly Arg Phe Gln Ser Pro Val Asp
        115                 120                 125

Ile Arg Pro Gln Leu Ala Ala Phe Cys Pro Ala Leu Arg Pro Leu Glu
    130                 135                 140
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195 200 205

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Ile Pro Ala Pro Ala Pro Gly Leu Thr Val Gln Leu Leu Leu Ser Leu
                -20                 -15                 -10

ctg ctt ctg atg cct gtc cat ccc cag agg ttg ccc cgg atg cag gag   147
Leu Leu Leu Met Pro Val His Pro Gln Arg Leu Pro Arg Met Gln Glu
             -5                  -1   1                   5

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Asp Ser Pro Leu Gly Gly Gly Ser Ser Gly Glu Asp Asp Pro Leu Gly
     10                  15                  20
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Glu Glu Asp Leu Pro Ser Glu Glu Asp Ser Pro Arg Glu Glu Asp Pro
 25                  30                  35                  40

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Pro Gly Glu Glu Asp Leu Pro Gly Glu Glu Asp Leu Pro Gly Glu Glu
             45                  50                  55

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         60                  65                  70

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 90                  95                 100

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Arg Tyr Gly Gly Asp Pro Pro Trp Pro Arg Val Ser Pro Ala Cys Ala
105                 110                 115                 120

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    170                 175                 180

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185                 190                 195                 200


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Glu His Thr Val Glu Gly His Arg Phe Pro Ala Glu Ile His Val Val
                205                 210                 215

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His Leu Ser Thr Ala Phe Ala Arg Val Asp Glu Ala Leu Gly Arg Pro
            220                 225                 230

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gcg ttc ctt gtg cag atg aga agg cag cac aga agg gga acc aaa ggg   1347
Ala Phe Leu Val Gln Met Arg Arg Gln His Arg Arg Gly Thr Lys Gly
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Gly Val Ser Tyr Arg Pro Ala Glu Val Ala Glu Thr Gly Ala
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tagaggctgg atcttggaga atgtgagaag ccagccagag gcatctgagg gggagccggt 1449

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    -20                 -15                 -10

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Gly Asp Pro Pro Trp Pro Arg Val Ser Pro Ala Cys Ala Gly Arg Phe
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Gln Ser Pro Val Asp Ile Arg Pro Gln Leu Ala Ala Phe Cys Pro Ala
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Thr Ala Phe Ala Arg Val Asp Glu Ala Leu Gly Arg Pro Gly Gly Leu
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Tyr Glu Gln Leu Leu Ser Arg Leu Glu Glu Ile Ala Glu Glu Gly Ser
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Glu Thr Gln Val Pro Gly Leu Asp Ile Ser Ala Leu Leu Pro Ser Asp
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Phe Ser Arg Tyr Phe Gln Tyr Glu Gly Ser Leu Thr Thr Pro Pro Cys
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Ala Lys Gln Leu His Thr Leu Ser Asp Thr Leu Trp Gly Pro Gly Asp
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Ser Arg Leu Gln Leu Asn Phe Arg Ala Thr Gln Pro Leu Asn Gly Arg
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Val Ile Glu Ala Ser Phe Pro Ala Gly Val Asp Ser Ser Pro Arg Ala
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Ala Glu Pro Val Gln Leu Asn Ser Cys Leu Ala Ala Gly Asp Ile Leu
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Ala Leu Val Phe Gly Leu Leu Phe Ala Val Thr Ser Val Ala Phe Leu
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